REMARKS

This Response to Office Action is filed in connection with the Office Action mailed September 8, 2006. Claims 31, 34 to 36, 38, 40, 43, 47, 49, 51, 54, 55, 71 to 73, 76, 78, 80, 82, 85 to 88 and 114 to 120 are pending. Claims 116, 117 and 120 have been cancelled herein without prejudice. Applicants maintain the right to prosecute the cancelled claims in any related application claiming the benefit of priority of the subject application. New claims 121 to 155 have been added. Accordingly, upon entry of the Response, claims 31, 34 to 36, 38, 40, 43, 47, 49, 51, 54, 55, 71 to 73, 76, 78, 80, 82, 85 to 88, 114, 115, 118, 119 and 121 to 155 are under consideration.

Regarding the Claim Amendments

The amendments to the claims are supported throughout the specification or were made to address informalities. In particular, the amendment to claims 31 and 71 to recite "contacting gastrointestinal mucosal tissue comprising K cells or stem cells, or multipotent progenitor cells that differentiate into K cells" is supported, for example, by claims 1, 17, 31, 52 and 67, as originally filed; at page 10, lines 25-28, which discloses K cells, and a mucosal cell that is "a stem cell or a pluripotent or multipotent progenitor cell;" and at page 25, lines 3-6, which discloses that:

> "a mucosal cell refers to the various cell types that normally reside in the aforementioned regions including stem cells or other multipotent or pluripotent cells that differentiate into the various mucosal cell types. Particular examples of mucosal cells include endocrine cells, such as K cells, L-cells, S-cells, G-cells, D-cells, I-cells, Mo-cells, Gr-cells and entero-endocrine cells."

This amendment to claims 31 and 71 is also supported, for example, at page 25, lines 24-25, which discloses that "K cell and stem cells" are target cells; at page 29, lines 7-8; and at page 30, lines 9-11. The amendment to claims 31 and 71 to recite polynucleotide "vector" is supported, for example, at page 11, line 7, to page 12, line 2; and page 12, lines 8-20. The amendment to claims 31 and 71 to recite "glucose, sucrose, fructose, carbohydrate" is supported, for example, at page 16, lines 1-6. The amendment to claims 31 and 71 to recite "increases" transcription or secretion is supported, for example, at page 19, lines 10-19. The amendment to claim 71 to recite "reducing blood

glucose" is supported, for example, at page 23, lines 10-12, which discloses that delivery from gut of leptin will enhance the clinical benefit of leptin reducing food intake and body mass "as well as blood glucose;" at page 33, lines 10-12, which discloses that disorders treatable include obesity or an undesirable body mass, and that leptin can "provide normal glucose homeostasis," and at page 35, lines 24-30, which discloses that an improvement in obesity is a "reduction of blood glucose." The amendment to claims 31 and 71 to refer back to the preamble of each respective claim was made to more clearly indicate that the method is effected. The amendment to claim 35 to recite the fasting plasma glucose greater than 110 mg/dl is "prior to treatment" was made to more clearly indicate the timing of treatment, and is also supported, for example, at page 36, lines 21-22, and page 36, line 29, to page 37, line 2. The amendment to claims 38 and 73 to recite that the "glucose increases transcription and secretion of the insulin by the transformed cells" is supported, for example, by originally filed claims 3, 4, 7, 38, 41 and 44 (see, also, page 9, line 25, to page 10, line 6). The amendment to claim 40 to recite that the "polypeptide or amino acid increases secretion of the insulin by transformed cells" is also supported, for example, by originally filed claims 3, and 38 (see, also, page 9, line 25, to page 10, line 6). The amendment to claims 43 and 76 was made in order to more clearly indicate promoter "transcription" function. The amendment to claims 47, 49, 51, 78, 80, 82, 118 and 119 to recite "....transformed K cells...." was made in order to provide greater antecedent basis for the referenced cells. The amendment to claims 54 and 85 was made in order to more clearly indicate the relationship of the promoter and nucleic acid encoding insulin or leptin to the vector. The amendment to claim 72 to recite that the "subject is obese" is supported, for example, at page 33, lines 10-11 and 21-22. The amendment to claims 87, 88, 114 and 115 to recite "contacting" instead of transforming was made in order to provide greater antecedent basis for the recited step. Thus, as the claim amendments are supported by the specification or were made to address informalities, no new matter has been added and, entry of the amendments is respectfully requested.

Regarding the New Claims

New claims 121 to 155 are supported throughout the specification. For example, claims 121 and 133 are directed to the subject matter of claims 31 and 71, respectively,

prior to the amendment to claims 31 and 71 deleting reference to the chromogranin A promoter and cells in which chromogranin A promoter functions. Claim 144 is directed to the subject matter of claim 31, except reciting a "proglucagon" promoter, which is supported, for example, at page 13, line 27, to page 14, line 7. Claims 122 to 132, which depend from claim 121 substantially parallel the subject matter of the claims that depend from claim 31. Claims 134 to 143, which depend from claim 133 substantially parallel the subject matter of the claims that depend from claim 71. Claims 145 to 155, which depend from claim 144 substantially parallel the subject matter of the claims that depend from claim 31. Claims 121 to 155 are also supported as set forth above for the claim amendments. Thus, as claims 121 to 155 are supported by the specification, no new matter has been added and entry thereof is respectfully requested.

I. OBJECTION TO CLAIMS

Claims 31 and 71 stand objected to due to claiming the same cell twice, namely, "pluripotent or multipotent progenitor cells." Allegedly, the subject matter is not distinct.

Applicants respectfully submit that pluripotent and multipotent progenitor cells are not the same cell. As is known in the relevant art, pluripotent cells have the potential to differentiate into any of the three germ layers: endoderm, mesoderm and ectoderm. Pluripotent stem cells can give rise to any fetal or adult cell type. In contrast, multipotent cells can give rise to different cell types, but those types are limited in diversity. For example, a multipotent hematopoietic cell is a blood stem cell that can develop into various types of blood cells, but does not develop into neural or other non-hematopoietic cells.

Nevertheless, solely in order to further prosecution of the applications and without acquiescing to the propriety of the rejection, the term "pluripotent" has been deleted from the claims. Accordingly, Applicants respectfully request that the objection be withdrawn.

II. REJECTION UNDER 35 U.S.C. §112, SECOND PARAGRAPH

The rejection of claims 31, 34 to 36, 38, 40, 43, 47, 49, 51, 54, 55, 71 to 73, 76, 78, 80, 82, 85 to 88 and 114 to 120 under 35 U.S.C. §112, second paragraph, as indefinite, is respectfully traversed. Allegedly, certain terms lack clarity." [Office Action, pages 3-6]

Claims 31, 34 to 36, 38, 40, 43, 47, 49, 51, 54, 55, 71 to 73, 76, 78, 80, 82, 85 to 88 and 114 to 120 are clear and definite prior to entry of the amendments set forth above. Nevertheless, solely in order to further prosecution of the application and without acquiescing to the propriety of the rejection, claims 116, 117 and 120 have been cancelled herein without prejudice and, therefore, the rejection as to these claims is moot. Claims 31 and 71, as amended, do not recite "gut mucosal tissue endocrine cells." Claims 31 and 71, as amended, more clearly indicate that the method has been effected, namely the concluding language more closely refers to the preamble. Claim 35, as amended, more clearly indicates the subjects have the recited fasting plasma glucose prior to treatment. Claims 43 and 76, as amended, more clearly indicate promoter function. Claims 54 and 85, as amended, more clearly indicate the relationship of the promoter and nucleic acid encoding insulin or leptin to the vector. None of the foregoing amendments were made for reasons related to patentability.

In terms of claims 71 and 72, and the meaning of "undesirable body mass," the specification discloses that "undesirable body mass" refers to subjects having 1%-29% greater body mass than a matched normal subject as well as subjects that are normal with respect to body mass but who wish to decrease or prevent an increase in their body mass." (page 33, lines 23-25) In view of the specification, one skilled in the art would clearly understand the metes and bounds of "undesirable body mass." To the extent that undesirable body mass may be partially subjective, this does not render the claims indefinite under 35 U.S.C. §112, second paragraph, since the skilled person in the relevant art would know which individuals subjectively have an undesirable body mass: such subjects would be those to undergo the claimed methods. As such, claims 71 and 72 are clear and definite.

In view of the amendments and remarks, claims 31, 34 to 36, 38, 40, 43, 47, 49, 51, 54, 55, 71 to 73, 76, 78, 80, 82, 85 to 88, 114, 115 and 118 to 120 are clear and definite. Accordingly, Applicants respectfully request that the rejection under 35 U.S.C. §112, second paragraph, be withdrawn.

III. REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH, WRITTEN DESCRIPTION

"Cell Types and Tissues"

The rejection of claims 47, 49, 78 and 80 under 35 U.S.C. §112, first paragraph, as allegedly lacking an adequate written description, is respectfully traversed. The grounds for rejection are as set forth in the Office Action, pages 6-7.

Claims 47, 49, 78 and 80 are adequately supported throughout the specification. As set forth above and in Applicants prior Response filed July 11, 2006, the specification adequately supports the recited cell types. In particular, for the sake of avoiding redundancy, Applicants respectfully direct the Examiner's attention to the specification which discloses that:

> "a mucosal cell refers to the various cell types that normally reside in the aforementioned regions including stem cells or other multipotent or pluripotent cells that differentiate into the various mucosal cell types. Particular examples of mucosal cells include endocrine cells, such as K cells, L-cells, S-cells, G-cells, D-cells, I-cells, Mo-cells, Gr-cells and entero-endocrine cells." (page 25, lines 3-6).

The "aforementioned regions" that the foregoing passage refers to includes:

> "cells which are normally found in animal mucosa, such as a cell of the gut (*e.g.*, mouth (tongue and buccal tissue), esophagus, and stomach, small and large intestine, rectum, anus), the respiratory tract, the lungs and nasopharynx and other oral cavities (*e.g.*, vagina)." (page 24, line 30, to page 25, line 3).

Thus, the specification adequately supports the recited cell types in the recited tissues. Consequently, this rejection under 35 U.S.C. §112, first paragraph is improper and must be withdrawn.

"Selective Transformation"

The rejection of claims 31, 34 to 36, 40, 43, 47, 49, 51, 54, 55, 71 to 73, 76, 78, 80, 82, 85 to 88 and 114 to 120 under 35 U.S.C. §112, first paragraph, as allegedly lacking an adequate written description, is respectfully traversed. The grounds for rejection are as set forth in the Office Action, pages 7-8.

Claims 116, 117 and 120 have been cancelled herein without prejudice. Consequently, the rejection is moot as to these claims.

Claims 31, 34 to 36, 40, 43, 47, 49, 51, 54, 55, 71 to 73, 76, 78, 80, 82, 85 to 88 and 114, 115 and 118 to 120 are adequately supported throughout the specification. The claims, both prior to after entry of this Response, never recited "selective" transformation. Thus, it is unclear why the claims have been rejected on the basis of selective transformation. Nevertheless, solely in order to further prosecution of the application and without acquiescing to the propriety of the rejection, the claims have been amended to delete "transforming" and to instead recite "contacting" gastrointestinal mucosal tissue,....wherein "contacting" occurs *in vivo* via intra cavity delivery....thereby producing "transformed" cells. Thus, the grounds for rejection are believed moot and Applicants respectfully request that the rejection under 35 U.S.C. §112, first paragraph be withdrawn.

Sugars and Other Types of Molecules

The rejection of claims 31, 34 to 36, 40, 43, 47 to 49, 51, 52, 54, 55, 71 to 73, 76, 78 to 80, 82, 83 and 85 to 88 under 35 U.S.C. §112, first paragraph, as allegedly lacking an adequate written description, is respectfully traversed. The grounds for rejection are as set forth in the Office Action, page 9.

Claims 31, 34 to 36, 40, 43, 47 to 49, 51, 52, 54, 55, 71 to 73, 76, 78 to 80, 82, 83 and 85 to 88 are adequately supported throughout the specification. Nevertheless, solely in order to further prosecution of the application and without acquiescing to the propriety of the rejection, the claims that reference GIP promoter have been amended, and recite "glucose, sucrose, fructose, carbohydrate, polypeptide, amino acid or fat."

The Examiner acknowledges that glucose, carbohydrates and fats induce transcription of GIP promoter. In terms of sucrose and fructose, in Exhibit E previously filed July 11, 2006, the authors report that oral administration of sugars including fructose and sucrose to ob/ob mice stimulated prompt (within 30 minutes) release of GIP. Thus, in view of previously submitted Exhibit E fructose and sucrose increase transcription of GIP promoter or secretion.

In terms of polypeptides or amino acids, in Exhibit F previously filed July 11, 2006, the authors report increased GIP release in response to duodenal instillation of amino acids. To further corroborate that polypeptides or amino acids can increase transcription or secretion of insulin operably linked to GIP promoter, submitted herewith

as Exhibit 1, is a publication by Wolfe *et al.* (Am. J. Gastrointest. Liver Physiol. 279:G561 (2000). The authors report that protein (peptone, a protein hydrosylate) stimulated GIP release in rats. Furthermore, the authors report that peptone did not significantly alter GIP RNA. Thus, in view of Exhibit 1, protein or amino acids increase GIP secretion without significant activation of the GIP promoter.

In view of the previously filed Exhibits E and F, and accompanying Exhibit 1, the specification adequately describes the nutrients, as recited in the claims, that can increase transcription or secretion of insulin operably linked to a GIP promoter. Accordingly, Applicants respectfully request withdrawal of this rejection under 35 U.S.C. §112, first paragraph.

IV. REJECTIONS UNDER 35 U.S.C. §112, FIRST PARAGRAPH, ENABLEMENT

The rejection of claims 31, 34 to 36, 38, 40, 43, 47, 49, 51, 54, 55, 87, 114, 116 and 118 under 35 U.S.C. §112, first paragraph, as allegedly lacking enablement is respectfully traversed. The grounds for rejection are as set forth in the Office Action, pages 10-27.

Claims 31, 34 to 36, 38, 40, 43, 47, 49, 51, 54, 55, 87, 114, 116 and 118 are adequately enabled. Nevertheless, solely in order to further prosecution of the application and without acquiescing to the propriety of the rejection, claim 116 has been cancelled herein without prejudice rendering the rejection of this claim moot, and the remaining claims have been amended as set forth above. The grounds for rejection will therefore be addressed with respect to the amended claims upon entry of this Response.

Transformation of Cells

As discussed above, the claims do not require selective cell contact. Furthermore, there is no requirement that non-target cells not be contacted or not have vector introduced. In the claimed methods, gastrointestinal mucosal tissue cells are contacted. Certain subpopulations of cells, such as K cells, other gut endocrine cells, or progenitor cells, become transformed. Upon feeding (consuming or ingesting) a recited nutrient to a subject, transformed K cells (GIP promoter) and transformed gut endocrine cells (chromogranin A promoter and proglucagon promoter) increase transcription or secretion of insulin or leptin from the cells. Such transformed cells, due to their natural function *in*

vivo produce, by virtue of increased transcription or increased secretion, insulin or leptin in response to the recited nutrients. Consequently, as the claimed methods do not require selective cell contact or that non-target cells not be contacted or not have vector introduced, these grounds for rejection are not applicable to the claimed methods.

Expression and Secretion

In terms of the assertion that transcription is not severable from secretion, Applicants recognize that there must be some amount of insulin or leptin transcription in transformed cells in order to be secretion of insulin or leptin protein by the cells. However, Applicants have repeatedly addressed this issue in the record and during the Interview. To reiterate, as disclosed in the specification at page 19, line 10, to page 20, line 12, a recited nutrient need not increase insulin or leptin transcription because transcription in transformed cells can already be at a (basal) level to provide the protein secreted in response to nutrient. As disclosed in the specification, such cell function is endocrine in nature- transcription of the insulin or leptin gene occurs without a nutrient, and the translated protein is stored in a vessicle or similar intacellular structure, and when a recited nutrient is ingested by a subject, insulin or leptin transformed cells secrete stored protein from the vessicle or similar intacellular structure. Thus, the skilled artisan knows that protein secretion can occur before or in the absence of increased transcription of a corresponding gene and therefore, increases in secretion need not be concurrent with increases in transcription.

To further corroborate Applicants' position, as illustrated in the Declaration under 37 C.F.R. §1.132 executed by Dr. Anthony Cheung, paragraph 11, and Exhibit B, panel C, previously filed July 11, 2006, human C-peptide, a by product of insulin, is rapidly produced within 15 minutes of oral glucose administration to animals transformed with a GIP-insulin bearing vector. The rapid insulin production and clearance of blood glucose indicates that glucose increases insulin secretion. In addition, as discussed above, the authors of Exhibit 1 submitted herewith report that amino acids or protein can increase GIP secretion without a corresponding increase in GIP transcription. Thus, in view of the foregoing, the recited nutrients need not increase transcription in order to increase protein secretion. Consequently, because transcription can be at levels already

adequate to provide or sustain the amount of protein secreted in response to a nutrient, increased transcription is not required for increased secretion.

Treatment Breadth

In terms of the assertion that "treatment" encompasses more than the increase of insulin levels in the blood in response to glucose..., the amended claims recite that the effect of treatment is "to decrease or to reduce blood glucose" in the subject. In this regard, the specification discloses and Applicants have provided corroborating data that insulin and leptin decrease or reduce blood glucose in treated subjects- see, for example, the Declaration under 37 C.F.R. §1.132 executed by Dr. Timothy Kieffer, filed June 18, 2003 (paragraphs 17 and 18, Figure 11). Accordingly, the claimed methods are adequately enabled for treatment of subjects to decrease or reduce blood glucose.

Treatment with GIP promoter Vectors

In terms of the assertion that K cells were the only cells known to have active GIP transcription, the amended claims that reference GIP promoter recite "transformed K cells or stem cells, or multipotent progenitor cells that differentiate into K cells." Accordingly, the claimed methods are adequately enabled for the recited transformed cells.

Chromogranin A Promoter Activity

In terms of the assertion that chromogranin A promoter is only active in particular cells of the GI tract, Applicants respectfully point out that chromogranin A promoter has been reported to be expressed by many different gut endocrine cells. To corroborate Applicants position, submitted herewith as Exhibit 2 is a publication by Rindi *et al.* (Ann. N.Y. Acad. Sci. 1014:1 (2004)). As illustrated in Table 1, column 4 (page 5) of Exhibit 2, chromogranin A (CgA) was detected in all gut endocrine cell types. Consequently, as chromogranin A is broadly expressed in gut endocrine cells, chromogranin A promoter will be broadly active in gut endocrine cells. Accordingly, the claimed methods are adequately enabled for chromogranin A promoter broadly active in gut endocrine cells.

Proglucagon Promoter Activity

In terms of new claims 144 to 155, which recite "proglucagon promoter," Applicants wish to direct the Examiner's attention to Exhibit 3, a publication by Theodorakis *et al.* (Am. J. Physiol. Endocrinol. Metab. 290:550 (2005)). In brief, the

authors report expression of proglucagon and GLP-1 in K-cells in human duodenum using immunohistochemistry and in-situ RT-PCR of laser-captured, single duodenal cells. The studies indicate that the proglucagon gene is expressed in K-cells and therefore, that proglucogon promoter can be used to express insulin in K-cells.

Intra-Cavity Delivery and Treatment of Stomach Cells

In terms of the assertion that the skilled artisan would not reasonably predict the nucleic acid vectors to transform cells of the stomach; by oral administration of a vector, Applicants respectfully point out that stomach cells can be transformed by contacting cells *in vivo* via intra-cavity delivery. To corroborate Applicants position, submitted herewith as Exhibit 4 is a data summary sheet and Figure 1. In brief, mice were fed a bolus of a chitosan-packaged non-viral DNA vector, in which insulin or SEAP gene expression was driven by the GIP promoter. Stomach mucosa was subsequently analyzed for insulin and SEAP gene expression levels. The data in Exhibit 4 (Figure 1) indicates that cells in stomach mucosa of mice were transformed when both vectors were delivered orally, and that both insulin and SEAP were expressed in stomach mucosa.

Thus, Exhibit 4 corroborates that 1) cells in stomach can be transformed; 2) cells can be transformed by oral delivery of vector; and 3) K cells are present and can be transformed in stomach. Accordingly, in view of the foregoing data and reasons of record, the claims are adequately enabled for oral vector delivery and transformation of cells in stomach, including K cells, *in vivo*.

Vectors

In terms of the assertion that the claims encompass many viral vectors, and that the skilled artisan would only reasonably predict that dsDNA or viral vectors to be efficacious in transforming cells, Applicants respectfully remind the Patent Office that the standard for enablement is whether one skilled in the art could practice the invention without undue experimentation- the fact that experimentation is complex does not necessarily make it undue. *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988). Satisfying the enablement requirement does not preclude the claims from encompassing non-functional embodiments; rather, the standard is whether a skilled person could determine which embodiments were conceived, but not yet made, would be inoperative or operative with expenditure of no more effort than is normally required in the art. *Atlas Powder Co. v.*

E.I. du Pont de Nemours & Co., 750 F.2d 1569 (Fed. Cir. 1984). Here, the claims are adequately enabled in view of the guidance in the specification, knowledge in the art at the time of the invention, and further in view of the corroborating data indicating that both viral (e.g., FIV, six AAV vectors) and non-viral vectors can be used to transform cells in order to effect the claimed methods.

Leptin Treatment of Obesity or Undesirable Body Mass

For the reasons of record, the claims directed to treating a mammalian subject having undesirable body mass or obesity, wherein the effect of said treatment is to reduce or mass, are adequately enabled. Nevertheless, solely in order to further prosecution of the application and without acquiescing to the propriety of the rejection, claims directed to leptin have been amended to recite "reducing blood glucose" as the effect of treatment. In this regard, the specification discloses that subjects can be treated as claimed with leptin thereby reducing levels of glucose. Furthermore, even in subjects that do not respond to leptin therapy by losing weight, such subjects can exhibit reduced levels of glucose and improved glucose homeostasis. To corroborate Applicants position, submitted herewith are Exhibits 5 and 6, publications by Javir *et al.* (Diabetes 54:1994 (2005)) and Cochran *et al.* (J. Clin. Endocrinol. Metab. 89:1548 (2004)), respectively. The authors of Exhibit 5 report that leptin significantly reduced body weight (from 61.8 ± 3.6 to 57.4 ± 3.4 kg; $P = 0.02$) and blood glucose levels (from 205 ± 19 to 126 ± 11 mg/dl; $P < 0.001$)- see, for example, abstract. The authors of Exhibit 6 report that leptin reduced fasting blood glucose levels by 40-60% (see, for example, abstract). Exhibits 6 and 7 therefore corroborate that the claims directed to leptin are adequately enabled for reducing blood glucose.

To further corroborate Applicants position, submitted herewith as Exhibit 7 is a publication by Pelleymounter *et al.* (Science 269:540 (1995)). The authors of Exhibit 7 report that a modest weight loss was observed in mice treated with 0.1 and 1 mg/kg/day dose (Figure 1A). Additionally, serum levels of glucose were reduced in these animals treated with the same dose of leptin (Figure 3A). Furthermore, in Buettner *et al.* (Am. J. Physiol. Endocrinol. Metab. 278:E563 (2000)), which was cited by the Examiner, the authors reported that delivery of leptin to diet-induced obese rats improved insulin sensitivity and plasma metabolic variables (Table 3 and Figure 4) despite the animals

exhibiting a modest or no change in body weight change (Figure 3). Consequently, the claims directed to leptin are adequately enabled for reducing blood glucose.

In view of the foregoing guidance in the specification and knowledge in the art, corroborated by the evidence of record and as submitted herewith, the skilled artisan could practice claims 31, 34 to 36, 38, 40, 43, 47, 49, 51, 54, 55, 71 to 73, 76, 78, 80, 82, 85 to 88 and 114 to 120 without undue experimentation. As such, the claims are adequately enabled and the rejection under 35 U.S.C. §112, first paragraph, is improper and must be withdrawn.

V. REJECTION UNDER 35 U.S.C. §103(a)

The rejection of claims 31, 34, 35, 38, 40, 43, 47, 49, 51, 54, 55, 87, 114, 116 and 118 under 35 U.S.C. §103(a) as allegedly unpatentable over During *et al.* (U.S. Patent No. 6,503,887) in view of Cheung *et al.* (Science 290:1959 (2000)) or Hocker *et al.* ((Gastroenterology 121:43 (2001)) is respectfully traversed.

The application claims priority to provisional application serial nos. 60/188,796 and 60/254,464, filed March 13, 2000 and December 8, 2000, respectively. Cheung *et al.* was published on December 8, 2000. Hocker *et al.* was published in 2001. Consequently, neither Cheung *et al.* (Science 290:1959 (2000)) nor Hocker *et al.* ((Gastroenterology 121:43 (2001)) are available as prior art against the claims of the application. During *et al.* (U.S. Patent No. 6,503,887) fails to teach or suggest each and every element of claims 31, 34, 35, 38, 40, 43, 47, 49, 51, 54, 55, 87, 114, 116 and 118. Accordingly, the rejection under 35 U.S.C. §103(a) is improper and Applicants respectfully request that it be withdrawn.

CONCLUSION

In summary, for the reasons set forth herein, Applicants maintain that claims 31, 34 to 36, 38, 40, 43, 47, 49, 51, 54, 55, 71 to 73, 76, 78, 80, 82, 85 to 88, 114, 115, 118, 119 and 121 to 155 clearly and patentably define the invention, respectfully request that the Examiner reconsider the various grounds set forth in the Office Action, and respectfully request the allowance of the claims which are now pending.

The Examiner is invited to contact the undersigned to arrange an Interview if any of the issues raised in the Office Action remain upon entry of this response. Applicant's representative can be reached at (858) 509-4065.

Please charge any fees associated with the submission of this paper to Deposit Account Number 03-3975. The Commissioner for Patents is also authorized to credit any over payments to the above-referenced Deposit Account.

Respectfully submitted,

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